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 NEWS  1          Web Page for STN Seminar Schedule - N. America
 NEWS  2  JAN 08  CHEMLIST enhanced with New Zealand Inventory of Chemicals
 NEWS  3  JAN 16  CA/CAplus Company Name Thesaurus enhanced and reloaded
 NEWS  4  JAN 16  IPC version 2007.01 thesaurus available on STN
 NEWS  5  JAN 16  WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
 NEWS  6  JAN 22  CA/CAplus updated with revised CAS roles
 NEWS  7  JAN 22  CA/CAplus enhanced with patent applications from India
 NEWS  8  JAN 29  PHAR reloaded with new search and display fields
 NEWS  9  JAN 29  CAS Registry Number crossover limit increased to 300,000 in
                  multiple databases
 NEWS 10  FEB 15  PATDPASPC enhanced with Drug Approval numbers
 NEWS 11  FEB 15  RUSSIAPAT enhanced with pre-1994 records
 NEWS 12  FEB 23  KOREAPAT enhanced with IPC 8 features and functionality
 NEWS 13  FEB 26  MEDLINE reloaded with enhancements
 NEWS 14  FEB 26  EMBASE enhanced with Clinical Trial Number field
 NEWS 15  FEB 26  TOXCENTER enhanced with reloaded MEDLINE
 NEWS 16  FEB 26  IFICDB/IFIPAT/IFIUDB reloaded with enhancements
 NEWS 17  FEB 26  CAS Registry Number crossover limit increased from 10,000
                  to 300,000 in multiple databases
 NEWS 18  MAR 15  WPIDS/WPIX enhanced with new FRAGHITSTR display format
 NEWS 19  MAR 16  CASREACT coverage extended
 NEWS 20  MAR 20  MARPAT now updated daily
 NEWS 21  MAR 22  LWPI reloaded
 NEWS 22  MAR 30  RDISCLOSURE reloaded with enhancements
 NEWS 23  APR 02  JICST-EPLUS removed from database clusters and STN
 NEWS 24  APR 30  GENBANK reloaded and enhanced with Genome Project ID field
 NEWS 25  APR 30  CHEMCATS enhanced with 1.2 million new records
 NEWS 26  APR 30  CA/CAplus enhanced with 1870-1889 U.S. patent records
 NEWS 27  APR 30  INPADOC replaced by INPADOCDB on STN
 NEWS 28  MAY 01  New CAS web site launched
 NEWS 29  MAY 08  CA/CAplus Indian patent publication number format defined
 NEWS 30  MAY 11  RDISCLOSURE on STN Easy enhanced with new search and display
                  fields
 NEWS EXPRESS  NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

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 NEWS IPC8     For general information regarding STN implementation of IPC 8
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FILE 'HOME' ENTERED AT 08:26:26 ON 15 MAY 2007

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 08:26:36 ON 15 MAY 2007

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 14 MAY 2007 HIGHEST RN 934733-40-1
DICTIONARY FILE UPDATES: 14 MAY 2007 HIGHEST RN 934733-40-1

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http://www.cas.org/support/stngen/stndoc/properties.html

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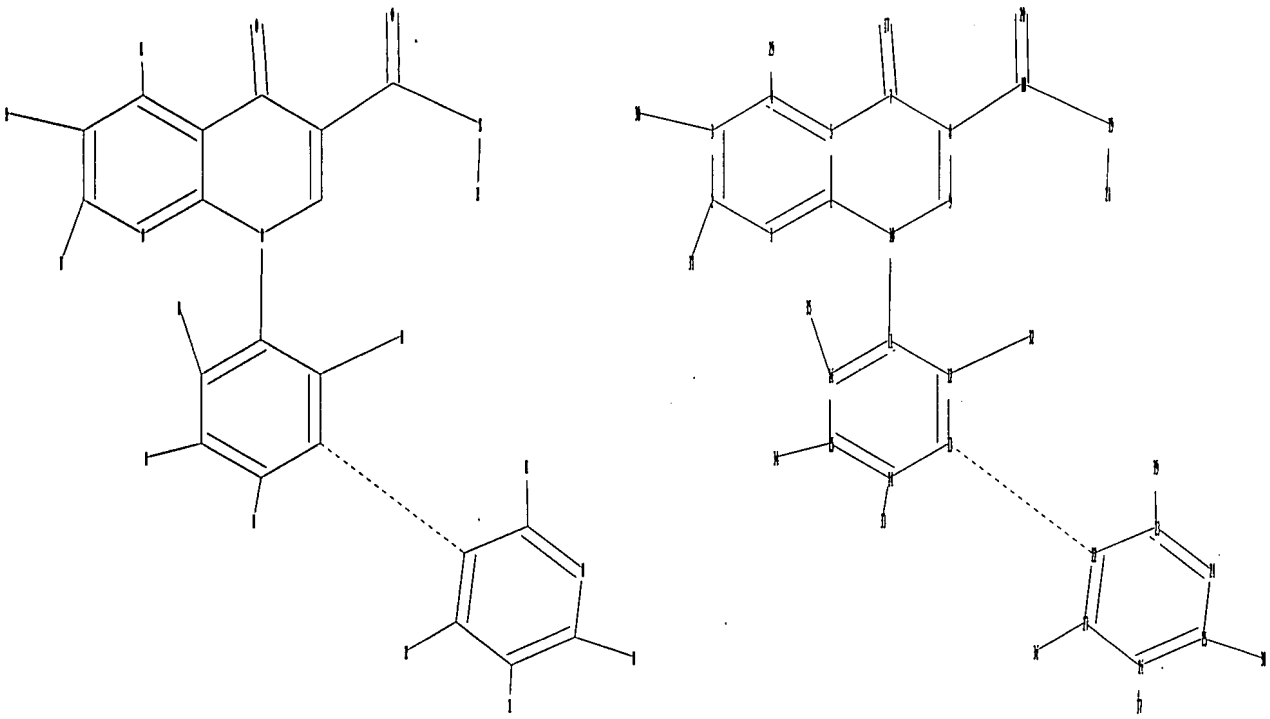

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17 18 19 20 21 29 30 31 32 33 34 35 36 37 38 39
ring nodes :
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chain bonds :
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18-20 19-21 23-39 25-38 26-37 27-36
ring bonds :
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14-15 15-16 22-23 22-27 23-24 24-25 25-26 26-27
exact/norm bonds :
5-7 6-10 7-8 7-17 8-9 9-10 10-11 13-22 18-19 18-20
exact bonds :
2-31 3-30 4-29 8-18 12-32 14-33 15-34 16-35 19-21 23-39 25-38 26-37
27-36
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 11-12 11-16 12-13 13-14 14-15 15-16 22-23
22-27 23-24 24-25 25-26 26-27
isolated ring systems :
containing 1 : 11 : 22 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:CLASS 18:CLASS 19:CLASS
20:CLASS 21:CLASS 22:Atom 23:Atom 24:Atom 25:Atom 26:Atom 27:Atom 29:CLASS
30:CLASS 31:CLASS 32:CLASS 33:CLASS 34:CLASS 35:CLASS 36:CLASS 37:CLASS
38:CLASS 39:CLASS

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L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.


=> s l1
SAMPLE SEARCH INITIATED 08:27:06 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -        2 TO ITERATE

100.0% PROCESSED        2 ITERATIONS                                 1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            2 TO      124
PROJECTED ANSWERS:               1 TO       80

L2            1 SEA SSS SAM L1

=> s l1 full
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100.0% PROCESSED       66 ITERATIONS                                 8 ANSWERS
SEARCH TIME: 00.00.01

L3            8 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   172.10     172.31

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FILE LAST UPDATED: 14 May 2007  (20070514/ED)

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=> s l3 full
L4            4 L3
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=> d ibib abs hitstr tot

L4 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:467891 CAPLUS
DOCUMENT NUMBER: 141:38597
TITLE: Preparation of aryl substituted 1,8-naphthyridin-4(1H)-ones as inhibitors of phosphodiesterase-4
INVENTOR(S): Albaneze-Walker, Jennifer; Murry, Jerry Anthony; Soheili, Arash; Springfield, Shawn A.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 142 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004048377	A2	20040610	WO 2003-US36806	20031118
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RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2506656	A1	20040610	CA 2003-2506656	20031118
AU 2003291050	A1	20040618	AU 2003-291050	20031118
EP 1565466	A2	20050824	EP 2003-783636	20031118
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003016464	A	20051011	BR 2003-16464	20031118
CN 1738818	A	20060222	CN 2003-80108946	20031118
JP 2006513271	T	20060420	JP 2005-510366	20031118
US 2006019981	A1	20060126	US 2005-530465	20050405
NO 2005003047	A	20050810	NO 2005-3047	20050621

PRIORITY APPLN. INFO.:	US 2002-428315P	P	20021122
	US 2003-472655P	P	20030522
	WO 2003-US36806	W	20031118

OTHER SOURCE(S): MARPAT 141:38597
GI

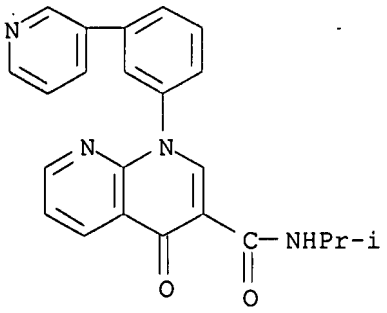
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB In one aspect, the present invention is directed to a one pot method of preparing intermediates I [OR1 = a suitable leaving group; R3 = (un)substituted alkyl, aryl, heteroaryl], which are useful in making inhibitors of phosphodiesterase-4. The present invention is also directed to a method of preparing phosphodiesterase inhibitors (no biol. data given) comprising the compds. II and III which comprises reacting IV [OR1 as above] with a 3-bromopyridine-N-oxide.HCl or 3-bromopyridine in the presence of a palladium catalyst and a phosphine ligand in amine base followed by reaction of the resulting V or VI with cyclopropylamine, optionally in the presence of catalyst. Thus, reacting IV [R1 = Et] with a 3-bromopyridine-N-oxide.HCl in the presence of [(allyl)PdCl]2, P(tert-Bu)3, tert-amylamine in DMAc followed by reacting V [R1 = Et] with

cyclopropylamine afforded II. Preparation of 77 aryl substituted 1,8-naphthyridin-4(1H)-ones and their intermediates is also described.

IT 477251-87-9P 477251-95-9P 694489-52-6P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of aryl substituted 1,8-naphthyridin-4(1H)-ones as inhibitors of phosphodiesterase-4)

RN 477251-87-9 CAPLUS
CN 1,8-Naphthyridine-3-carboxamide, 1,4-dihydro-N-(1-methylethyl)-4-oxo-1-[3-(3-pyridinyl)phenyl]- (9CI) (CA INDEX NAME)



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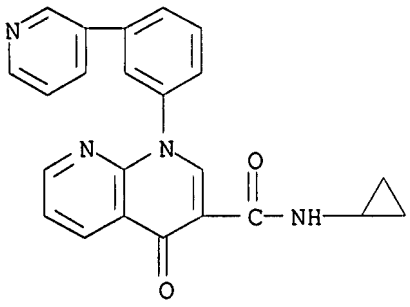

RN 694489-52-6 CAPLUS
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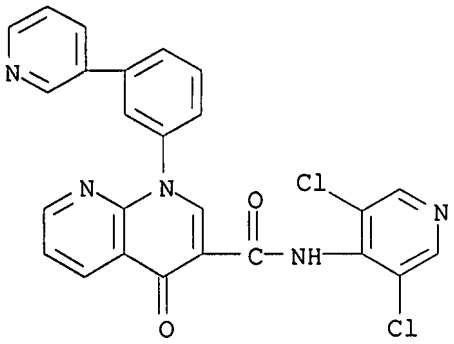
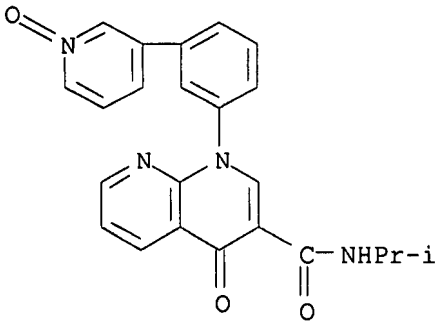


IT 477252-44-1P 477252-50-9P 694489-58-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aryl substituted 1,8-naphthyridin-4(1H)-ones as inhibitors of phosphodiesterase-4)

RN 477252-44-1 CAPLUS
CN 1,8-Naphthyridine-3-carboxamide, 1,4-dihydro-N-(1-methylethyl)-1-[3-(1-oxido-3-pyridinyl)phenyl]-4-oxo- (9CI) (CA INDEX NAME)



RN 477252-50-9 CAPLUS
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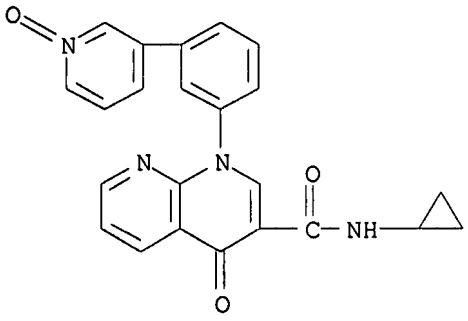

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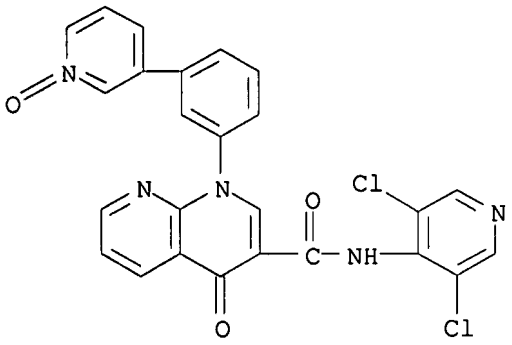

L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:467741 CAPLUS
DOCUMENT NUMBER: 141:38595
TITLE: Preparation of substituted naphthyridine

phosphodiesterase-4 inhibitors as enhancers of cognition

INVENTOR(S): Dube, Daniel; Gallant, Michel; Lacombe, Patrick; Girard, Yves; MacDonald, Dwight; Friesen, Richard; Ducharme, Yves; Cote, Bernard; Blouin, Marc; Martins, Evelyn; Guay, Daniel; Girard, Mario; Frenette, Richard; Laliberte, Sebastien; Robichaud, Annette; Mastracchio, Anthony; Perrier, Helene

PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.; Hamel, Pierre

SOURCE: PCT Int. Appl., 138 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004047836	A1	20040610	WO 2003-CA1799	20031119
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RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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EP 1592419	A1	20051109	EP 2003-776698	20031119
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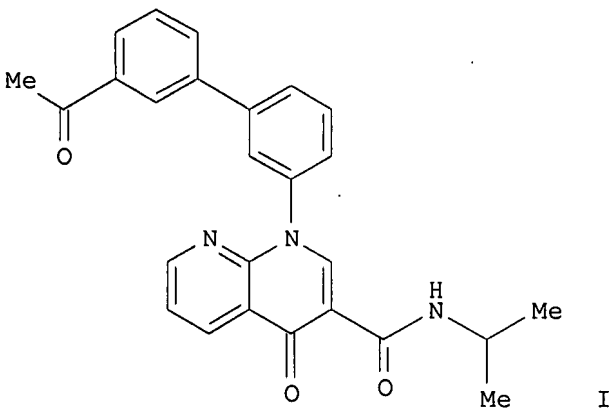
PRIORITY APPLN. INFO.: US 2002-428541P P 20021122
WO 2003-CA1799 W 20031119

GI



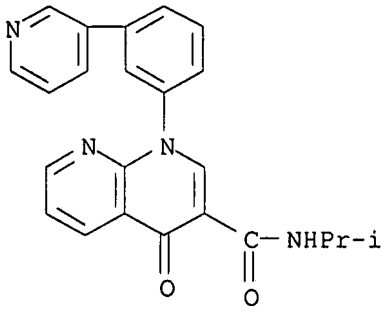
I

AB Substituted naphthyridines are prepared as PDE-4 inhibitors. For instance, Et 3-(3-bromoanilino)-2-(2-chloronicotinoyl)acrylate (preparation given) is treated with NaH in THF to give Et 1-(3-bromophenyl)-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxylate. This intermediate is saponified, coupled to i-PrNH2 (THF, Et3N, i-BuOCOCl) and coupled to 3-acetylphenylboronic acid (PhMe, EtOH, Na2CO3, trans-

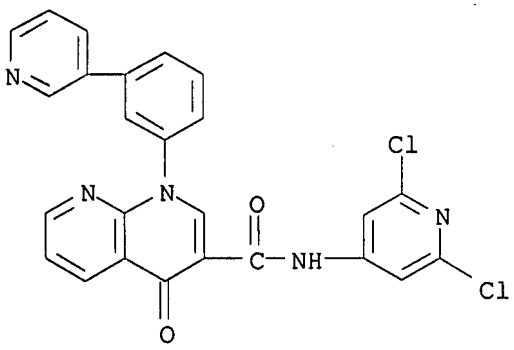
dibromobis(triphenylphosphine)palladium, reflux, 1 h) to give I. Example compds. have IC50 values of 0.1 to 90.0 nM for PDE4; these compds. are useful for enhancing memory, learning, retention, recall, awareness and judgement.

IT 477251-87-9P, N-Isopropyl-1-[3-(pyridin-3-yl)phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide 477251-91-5P, N-(2,6-Dichloropyridin-4-yl)-1-[3-(pyridin-3-yl)phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide 477251-95-9P, N-Cyclopropyl-1-[3-(pyridin-3-yl)phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of substituted naphthyridine phosphodiesterase-4 inhibitors as enhancers of cognition)

RN 477251-87-9 CAPLUS
CN 1,8-Naphthyridine-3-carboxamide, 1,4-dihydro-N-(1-methylethyl)-4-oxo-1-[3-(3-pyridinyl)phenyl]- (9CI) (CA INDEX NAME)



RN 477251-91-5 CAPLUS
CN 1,8-Naphthyridine-3-carboxamide, N-(2,6-dichloro-4-pyridinyl)-1,4-dihydro-4-oxo-1-[3-(3-pyridinyl)phenyl]- (9CI) (CA INDEX NAME)



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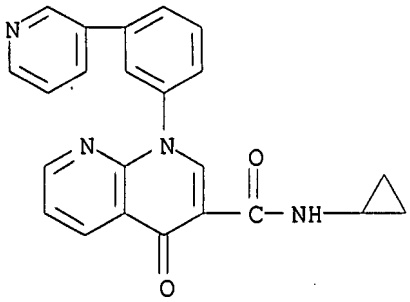
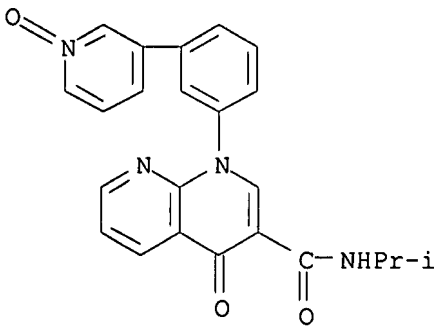


IT 477252-44-1P, N-Isopropyl-1-[3-(1-oxidopyridin-3-yl)phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide 477252-45-2P, N-(2,6-Dichloropyridin-4-yl)-1-[3-(1-oxidopyridin-3-yl)phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide 477252-50-9P, N-Cyclopropyl-1-[3-(1-oxidopyridin-3-yl)phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted naphthyridine phosphodiesterase-4 inhibitors as enhancers of cognition)

RN 477252-44-1 CAPLUS
CN 1,8-Naphthyridine-3-carboxamide, 1,4-dihydro-N-(1-methylethyl)-1-[3-(1-oxido-3-pyridinyl)phenyl]-4-oxo- (9CI) (CA INDEX NAME)



RN 477252-45-2 CAPLUS
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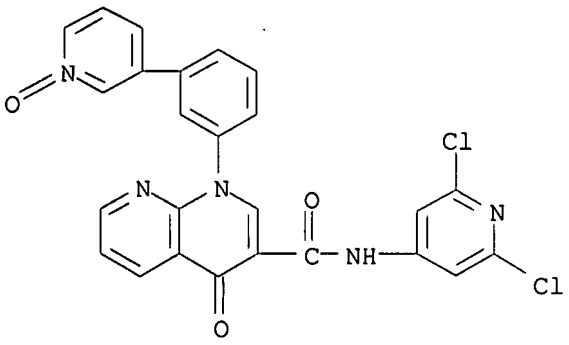

RN 477252-50-9 CAPLUS
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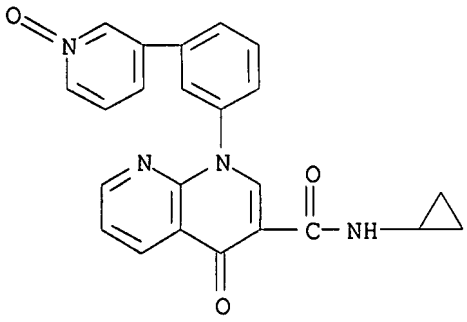


REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:433770 CAPLUS
DOCUMENT NUMBER: 141:7041
TITLE: One-pot preparation of naphthyridine derivatives, useful as inhibitors of phosphodiesterase-4
INVENTOR(S): Albaneze-Walker, Jennifer; Ceglia, Scott; Murry, Jerry Anthony; Soheili, Arash
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 57 pp., which
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

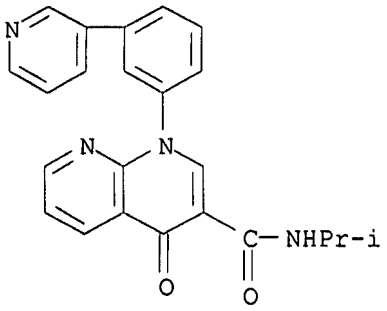
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004102472	A1	20040527	US 2003-690118		20031021
US 6909002	B2	20050621			
PRIORITY APPLN. INFO.:			US 2002-428315P	P	20021122
			US 2003-472598P	P	20030522

OTHER SOURCE(S): CASREACT 141:7041; MARPAT 141:7041
GI

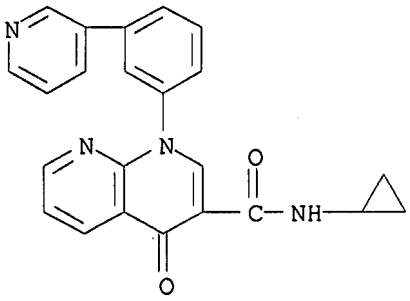
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to one-pot preparation of naphthyridine derivs. of formula I [wherein: OR1 is a suitable leaving group; R2 is C1-8alkyl, (un)substituted (hetero)aryl], useful as inhibitors of phosphodiesterase-4 (no biol. data). For instance, naphthyridine derivative II was prepared via heterocyclization of Et 2-chloronicotinoylacetate, 3-bromoaniline, and acetic anhydride, hydrolysis of the obtained ester III (R3 = Br), amidation by isopropylamine, and subsequent phenylacetylation by 3-acetylphenylboronic acid (example 1, no yield data). Naphthyridine derivative IV was prepared using the prepared intermediate III [R3 = -B(OH)2] (p. 49-53).
IT 477251-87-9P 477251-95-9P 694489-52-6P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(one-pot method of preparation of naphthyridine derivs. useful as inhibitors of phosphodiesterase-4)
RN 477251-87-9 CAPLUS

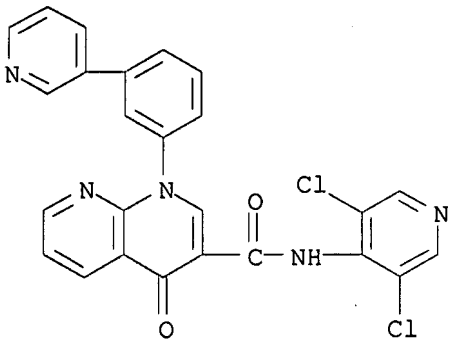
CN 1,8-Naphthyridine-3-carboxamide, 1,4-dihydro-N-(1-methylethyl)-4-oxo-1-[3-(3-pyridinyl)phenyl]- (9CI) (CA INDEX NAME)



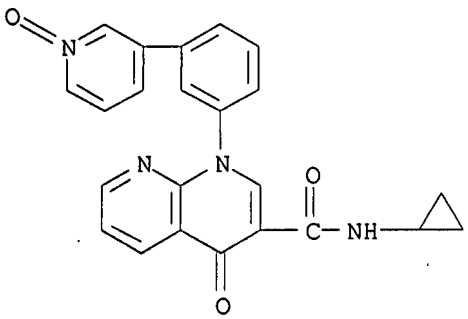
RN 477251-95-9 CAPLUS
CN 1,8-Naphthyridine-3-carboxamide, N-cyclopropyl-1,4-dihydro-4-oxo-1-[3-(3-pyridinyl)phenyl]- (9CI) (CA INDEX NAME)



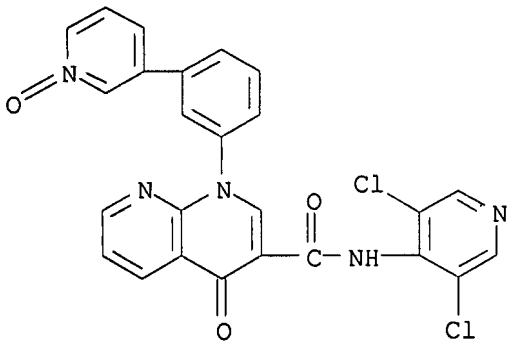
RN 694489-52-6 CAPLUS
CN 1,8-Naphthyridine-3-carboxamide, N-(3,5-dichloro-4-pyridinyl)-1,4-dihydro-4-oxo-1-[3-(3-pyridinyl)phenyl]- (9CI) (CA INDEX NAME)



IT 477252-50-9P 694489-58-2P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(one-pot preparation of naphthyridine derivs., useful as inhibitors of phosphodiesterase-4)
RN 477252-50-9 CAPLUS
CN 1,8-Naphthyridine-3-carboxamide, N-cyclopropyl-1,4-dihydro-1-[3-(1-oxido-3-pyridinyl)phenyl]-4-oxo- (9CI) (CA INDEX NAME)



RN 694489-58-2 CAPLUS
CN 1,8-Naphthyridine-3-carboxamide, N-(3,5-dichloro-4-pyridinyl)-1,4-dihydro-1-[3-(1-oxido-3-pyridinyl)phenyl]-4-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

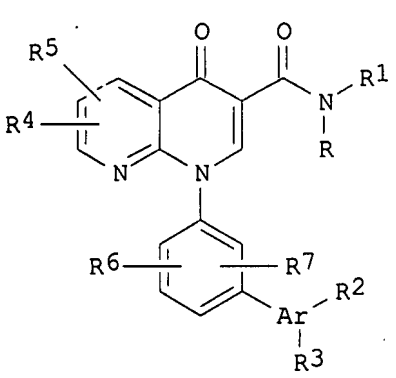
L4 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:906219 CAPLUS
DOCUMENT NUMBER: 138:4594
TITLE: Preparation of 1-biaryl-[1,8]naphthyridin-4-one phosphodiesterase IV inhibitors for treatment of asthma and inflammation
INVENTOR(S): Guay, Daniel; Girard, Mario; Hamel, Pierre; Laliberte, Sebastien; Friesen, Richard; Girard, Yves; Li, Chun
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 166 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002094823	A1	20021128	WO 2002-CA746	20020522
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2447765	A1	20021128	CA 2002-2447765	20020522

AU 2002257459	A1	20021203	AU 2002-257459		20020522
EP 1397359	A1	20040317	EP 2002-727127		20020522
EP 1397359	B1	20050831			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004534773	T	20041118	JP 2002-591496		20020522
AT 303384	T	20050915	AT 2002-727127		20020522
ES 2247325	T3	20060301	ES 2002-2727127		20020522
US 2003096829	A1	20030522	US 2002-154591		20020524
US 6677351	B2	20040113			
PRIORITY APPLN. INFO.:			US 2001-293247P	P	20010524
			WO 2002-CA746	W	20020522

OTHER SOURCE(S): MARPAT 138:4594

GI



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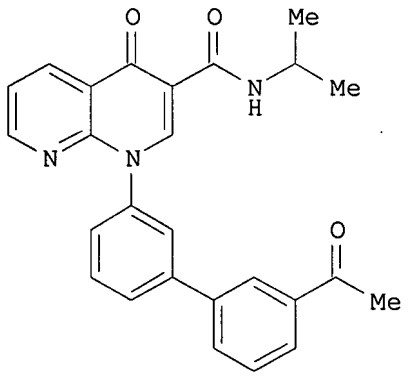


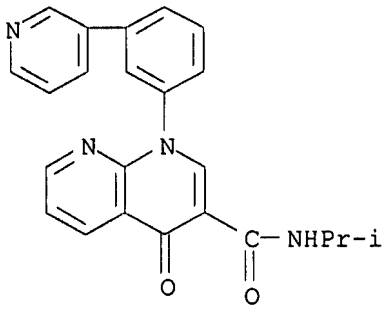
II

AB Title compds. I [wherein Ar = Ph, pyridyl, pyrimidyl, indolyl, quinolinyl, thienyl, pyridonyl, oxazolyl, oxadiazolyl, thiadiazolyl, imidazolyl, or heteroaryl oxides; R = H or alkyl; R1 = H or (un)substituted (cyclo)alkyl, alkoxy, alkenyl, alkynyl, heteroaryl, or heterocyclyl; R2 = H, halo, (cyclo)alkyl, alkoxy, amino, acyl, alkoxycarbonyl, alkylsulfamoyl, alkylsulfonyl, or (un)substituted Ph, heteroaryl, or heterocyclyl, etc.; R3 = H, OH, NH2, halo, (un)substituted alkyl; R4-R7 = independently H, halo, NH2, or (un)substituted alkyl or alkoxy; or pharmaceutically acceptable salts thereof] were prepared as phosphodiesterase IV (PDE4) inhibitors for the treatment of asthma and inflammation. For instance, Et 3-(3-bromoanilino)-2-(2-chloronicotinoyl)acrylate was cyclized using NaH in THF and the resulting ester saponified to give 1-(3-bromophenyl)-1,4-dihydro-[1,8]naphthyridin-4-one-3-carboxylic acid. Amidation with isopropylamine, followed by treatment with 3-acetylphenylboronic acid in the presence of trans-PdBr2(PPh3)2 and Na2CO3 in toluene and EtOH gave II. I demonstrated PDE4 inhibitory activity by suppression of TNF-α secretion in LPS stimulated human blood with IC50 values generally ranging from 0.005 μM to 15.4 μM. In a SPA based PDE activity assay, I inhibited the hydrolysis of cAMP to AMP by human recombinant phosphodiesterase IVa with IC50 values between 34.3 nM and 134.0 nM.

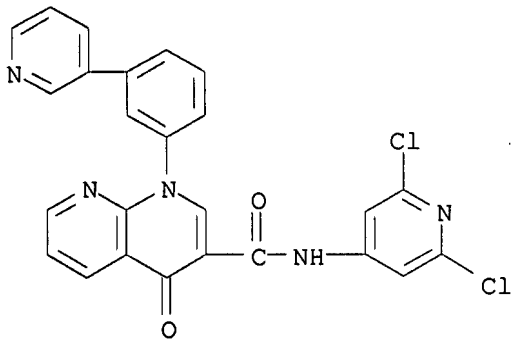
IT 477251-87-9P, N-Isopropyl-1-[3-(pyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477251-91-5P, N-(2,6-Dichloropyridin-4-yl)-1-[3-(pyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477251-95-9P, N-Cyclopropyl-1-[3-(pyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(PDE4 inhibitor; preparation of biarylnaphthyridinone PDE4 inhibitors by cyclization and arylation of (arylamino)(nicotinoyl)acrylates for treatment of asthma and inflammation)

RN 477251-87-9 CAPLUS

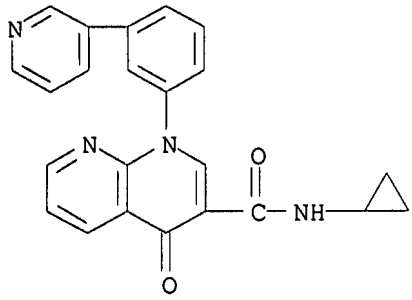
CN 1,8-Naphthyridine-3-carboxamide, 1,4-dihydro-N-(1-methylethyl)-4-oxo-1-[3-(3-pyridinyl)phenyl]- (9CI) (CA INDEX NAME)



RN 477251-91-5 CAPLUS
CN 1,8-Naphthyridine-3-carboxamide, N-(2,6-dichloro-4-pyridinyl)-1,4-dihydro-4-oxo-1-[3-(3-pyridinyl)phenyl]- (9CI) (CA INDEX NAME)

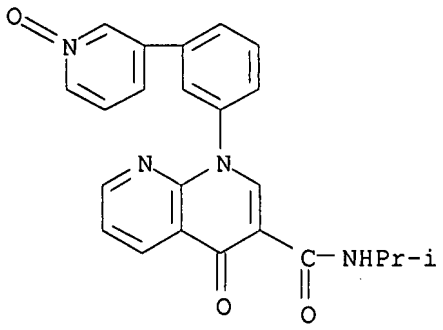


RN 477251-95-9 CAPLUS
CN 1,8-Naphthyridine-3-carboxamide, N-cyclopropyl-1,4-dihydro-4-oxo-1-[3-(3-pyridinyl)phenyl]- (9CI) (CA INDEX NAME)

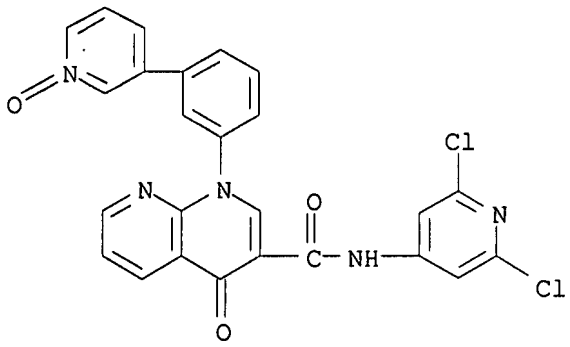


IT 477252-44-1P, N-Isopropyl-1-[3-(1-oxidopyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-45-2P, N-(2,6-Dichloropyridin-4-yl)-1-[3-(1-oxidopyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-50-9P, N-Cyclopropyl-1-[3-(1-oxidopyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(PDE4 inhibitor; preparation of biarylnaphthyridinone PDE4 inhibitors by cyclization and arylation of (arylamino)(nicotinoyl)acrylates for

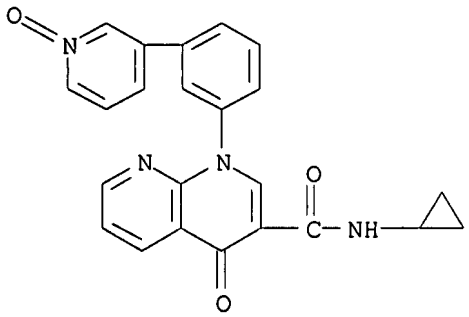
treatment of asthma and inflammation)
RN 477252-44-1 CAPLUS
CN 1,8-Naphthyridine-3-carboxamide, 1,4-dihydro-N-(1-methylethyl)-1-[3-(1-oxido-3-pyridinyl)phenyl]-4-oxo- (9CI) (CA INDEX NAME)



RN 477252-45-2 CAPLUS
CN 1,8-Naphthyridine-3-carboxamide, N-(2,6-dichloro-4-pyridinyl)-1,4-dihydro-1-[3-(1-oxido-3-pyridinyl)phenyl]-4-oxo- (9CI) (CA INDEX NAME)



RN 477252-50-9 CAPLUS
CN 1,8-Naphthyridine-3-carboxamide, N-cyclopropyl-1,4-dihydro-1-[3-(1-oxido-3-pyridinyl)phenyl]-4-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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(FILE 'HOME' ENTERED AT 08:26:26 ON 15 MAY 2007)

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L3            8 S L1 FULL

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L4            4 S L3 FULL

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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
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FULL ESTIMATED COST                                      22.49     194.80

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                      -3.12      -3.12

STN INTERNATIONAL LOGOFF AT 08:29:13 ON 15 MAY 2007
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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS 3	JAN 16	CA/CAplus Company Name Thesaurus enhanced and reloaded
NEWS 4	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS 5	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS 6	JAN 22	CA/CAplus updated with revised CAS roles
NEWS 7	JAN 22	CA/CAplus enhanced with patent applications from India
NEWS 8	JAN 29	PHAR reloaded with new search and display fields
NEWS 9	JAN 29	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS 10	FEB 15	PATDPASPC enhanced with Drug Approval numbers
NEWS 11	FEB 15	RUSSIAPAT enhanced with pre-1994 records
NEWS 12	FEB 23	KOREAPAT enhanced with IPC 8 features and functionality
NEWS 13	FEB 26	MEDLINE reloaded with enhancements
NEWS 14	FEB 26	EMBASE enhanced with Clinical Trial Number field
NEWS 15	FEB 26	TOXCENTER enhanced with reloaded MEDLINE
NEWS 16	FEB 26	IFICDB/IFIPAT/IFIUDB reloaded with enhancements
NEWS 17	FEB 26	CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases
NEWS 18	MAR 15	WPIDS/WPIX enhanced with new FRAGHITSTR display format
NEWS 19	MAR 16	CASREACT coverage extended
NEWS 20	MAR 20	MARPAT now updated daily
NEWS 21	MAR 22	LWPI reloaded
NEWS 22	MAR 30	RDISCLOSURE reloaded with enhancements
NEWS 23	APR 02	JICST-EPLUS removed from database clusters and STN
NEWS 24	APR 30	GENBANK reloaded and enhanced with Genome Project ID field
NEWS 25	APR 30	CHEMCATS enhanced with 1.2 million new records
NEWS 26	APR 30	CA/CAplus enhanced with 1870-1889 U.S. patent records
NEWS 27	APR 30	INPADOC replaced by INPADOCDB on STN
NEWS 28	MAY 01	New CAS web site launched
NEWS 29	MAY 08	CA/CAplus Indian patent publication number format defined
NEWS 30	MAY 11	RDISCLOSURE on STN Easy enhanced with new search and display fields
NEWS EXPRESS		NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.
NEWS HOURS		STN Operating Hours Plus Help Desk Availability
NEWS LOGIN		Welcome Banner and News Items
NEWS IPC8		For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 08:31:50 ON 15 MAY 2007

=> file caplus
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'CAPLUS' ENTERED AT 08:32:01 ON 15 MAY 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 15 May 2007 VOL 146 ISS 21
FILE LAST UPDATED: 14 May 2007 (20070514/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

=> file casreact
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.47	0.68

FILE 'CASREACT' ENTERED AT 08:32:07 ON 15 MAY 2007
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT

FILE CONTENT:1840 - 12 May 2007 VOL 146 ISS 21

New CAS Information Use Policies, enter HELP USAGETERMS for details.

****
*
* CASREACT now has more than 12 million reactions *
*
****

Some CASREACT records are derived from the ZIC/VINITI database (1974-1999) provided by InfoChem, INPI data prior to 1986, and Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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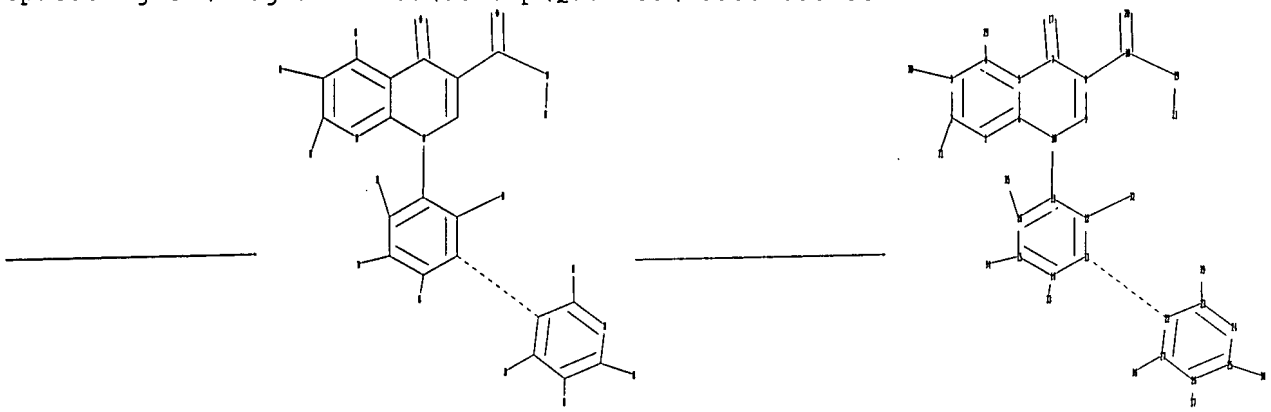

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ring nodes :
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chain bonds :
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18-20 19-21 23-39 25-38 26-37 27-36
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10 11-12 11-16 12-13 13-14
14-15 15-16 22-23 22-27 23-24 24-25 25-26 26-27
exact/norm bonds :
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exact bonds :
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27-36
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isolated ring systems :
containing 1 : 11 : 22 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:CLASS 18:CLASS 19:CLASS
20:CLASS 21:CLASS 22:Atom 23:Atom 24:Atom 25:Atom 26:Atom 27:Atom 29:CLASS
30:CLASS 31:CLASS 32:CLASS 33:CLASS 34:CLASS 35:CLASS 36:CLASS 37:CLASS
38:CLASS 39:CLASS
fragments assigned product role:
containing 1

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> s l1 full
FULL SEARCH INITIATED 08:32:44 FILE 'CASREACT'
SCREENING COMPLETE - 160 REACTIONS TO VERIFY FROM 3 DOCUMENTS

100.0% DONE 160 VERIFIED 22 HIT RXNS 1 DOCS
SEARCH TIME: 00.00.01

L2 1 SEA SSS FUL L1 (22 REACTIONS)

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L2 ANSWER 1 OF 1 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 141:7041 CASREACT
TITLE: One-pot preparation of naphthyridine derivatives, useful as inhibitors of phosphodiesterase-4
INVENTOR(S): Albaneze-Walker, Jennifer; Ceglia, Scott; Murry, Jerry Anthony; Soheili, Arash
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 57 pp., which
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

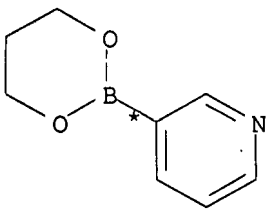
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004102472	A1	20040527	US 2003-690118	20031021
US 6909002	B2	20050621		

PRIORITY APPLN. INFO.: US 2002-428315P 20021122
US 2003-472598P 20030522
OTHER SOURCE(S): MARPAT 141:7041
GI

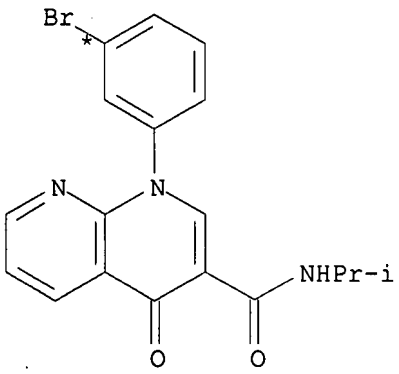
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to one-pot preparation of naphthyridine derivs. of formula I [wherein: OR1 is a suitable leaving group; R2 is C1-8alkyl, (un)substituted (hetero)aryl], useful as inhibitors of phosphodiesterase-4 (no biol. data). For instance, naphthyridine derivative II was prepared via heterocyclization of Et 2-chloronicotinoylacetate, 3-bromoaniline, and acetic anhydride, hydrolysis of the obtained ester III (R3 = Br), amidation by isopropylamine, and subsequent phenylacetylation by 3-acetylphenylboronic acid (example 1, no yield data). Naphthyridine derivative IV was prepared using the prepared intermediate III [R3 = -B(OH)2] (p. 49-53).

RX(12) OF 305 ...AL + B ===> AM



AL



B

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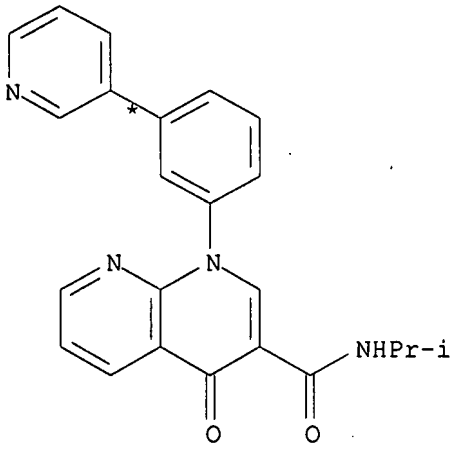

AM

RX(12) RCT AL 131534-65-1, B 477251-79-9
RGT D 497-19-8 Na2CO3
PRO AM 477251-87-9
CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-κP)ferrocene]dichloro-, (SP-4-2)-
SOL 7732-18-5 Water, 64-17-5 EtOH
CON 1 hour, reflux
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 08:31:50 ON 15 MAY 2007)

FILE 'CAPLUS' ENTERED AT 08:32:01 ON 15 MAY 2007

FILE 'CASREACT' ENTERED AT 08:32:07 ON 15 MAY 2007
L1 STRUCTURE UPLOADED
L2 1 S L1 FULL

=> log y
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION

FULL ESTIMATED COST	118.92	119.60
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.73	-0.73

STN INTERNATIONAL LOGOFF AT 08:33:19 ON 15 MAY 2007

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=> s l3
L4            7 L3

=> d abs bib fhitstr 1-7

L4   ANSWER 1 OF 7  CAPLUS  COPYRIGHT 2007 ACS on STN
AB   This invention relates to dry power aerosol formulations for use with a
     dry powder inhaler, the formulation comprising the PDE 4 inhibitor
     N-cyclopropyl-1-[3-(1-oxido-3-pyridinylethynyl)phenyl]-1,4-
     dihydro[1,8]naphthyridin-4-one-3-carboxamide.  An investigation into the
     aerosol performance of the above drug with different grades of lactose at
     4% drug loading demonstrated that sieved lactose was the most suitable
     carrier of the 3 choices.  Granulated lactose produced the weakest drug
     aerosolization compared to milled and sieved lactose.
AN   2007:356793  CAPLUS
DN   146:323609
TI   Aerosol powder formulation
IN   Thibert, Roch; Meisner, Dale; Rossi, Joanna; Tanfara, Helen
PA   Can.
SO   U.S. Pat. Appl. Publ., 10pp.
     CODEN: USXXCO
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
     ---------------     ----   --------    --------------------    --------
PI   US 2007071692        A1    20070329    US 2006-528107          20060927
     WO 2007036029        A1    20070405    WO 2006-CA1583          20060926
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             GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP,
             KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN,
             MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS,
             RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
PRAI US 2005-721402P      P     20050928
IT   500355-52-2, N-Cyclopropyl-1-[3-(1-oxido-3-
     pyridinylethynyl)phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide
     RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU
     (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
        (aerosol powder formulation)
RN   500355-52-2  CAPLUS
CN   1,8-Naphthyridine-3-carboxamide, N-cyclopropyl-1,4-dihydro-1-[3-[2-(1-
     oxido-3-pyridinyl)ethynyl]phenyl]-4-oxo-  (CA INDEX NAME)
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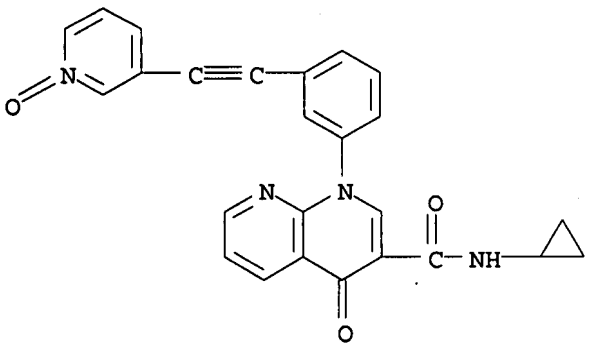
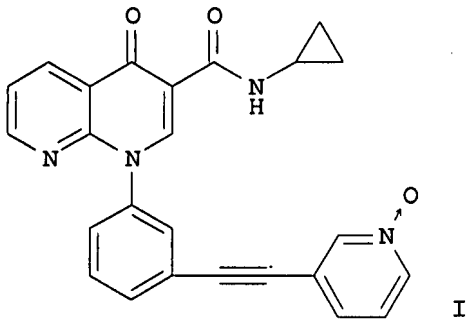


L4 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
GI



I

AB The present invention is directed to alternative forms of the title phosphodiesterase 4 inhibitor (I). I was prepared from Et 4-oxo-1,4-dihydro-4-(3-ethynylphenyl)-1,8-naphthyridine-3-carboxylate and 3-bromopyridine N-oxide giving an ester which was then treated with cyclopropylamine. Polymorphic forms such as the hemihydrate, anhydrous form, dihydrate, and monohydrate were prepared

AN 2005:1200294 CAPLUS
DN 143:460135
TI Preparation of polymorphic forms of the phosphodiesterase-4 inhibitor N-cyclopropyl-1-{3-[(1-oxidopyridin-3-yl)ethynyl]phenyl}-4-oxo-1,4-dihydro-1,8-naphthyridine-3-carboxamide
IN Clas, Sophie-Dorothee; Naccache, Rafik; Yu, Hongshi; Murry, Jerry; Variankaval, Narayan
PA Merck Frosst Canada Ltd., Can.; Merck & Co., Inc.
SO PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005105084	A1	20051110	WO 2005-US13853	20050422

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,

GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1742628 A1 20070117 EP 2005-738340 20050422

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR

PRAI US 2004-565446P P 20040426

WO 2005-US13853 W 20050422

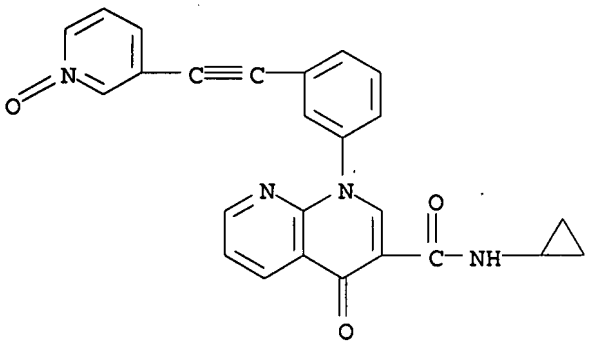
IT 500355-52-2P

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of polymorphic forms of phosphodiesterase-4 inhibitor N-cyclopropyl-1-{3-[(1-oxidopyridin-3-yl)ethynyl]phenyl}-4-oxo-1,4-dihydro-1,8-naphthyridine-3-carboxamide)

RN 500355-52-2 CAPLUS

CN 1,8-Naphthyridine-3-carboxamide, N-cyclopropyl-1,4-dihydro-1-[3-[2-(1-oxido-3-pyridinyl)ethynyl]phenyl]-4-oxo- (CA INDEX NAME)



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN

AB The invention discloses the treatment or prevention of diseases involving deposition of β-amyloid in the brain, e.g. Alzheimer's disease, via the combined administration of a growth hormone secretagogue and a PDE4 inhibitor.

AN 2004:857402 CAPLUS

DN 141:325764

TI Growth hormone secretagogue-phosphodiesterase 4 inhibitor combination for the treatment of Alzheimer's disease

IN Castro Pineiro, Jose Luis

PA Merck Sharp & Dohme Limited, UK

SO PCT Int. Appl., 20 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004087157	A2	20041014	WO 2004-GB1435	20040401
	WO 2004087157	A3	20041118		
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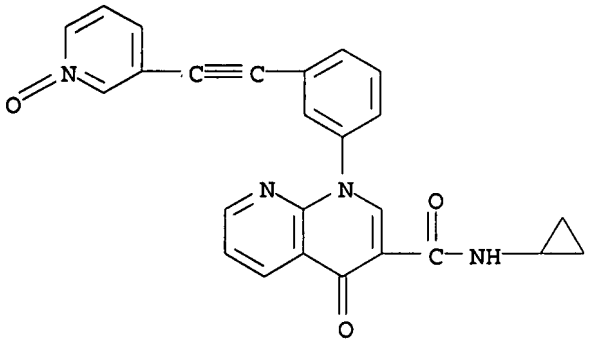
	AU 2004226698	A1	20041014	AU 2004-226698	20040401
	CA 2521046	A1	20041014	CA 2004-2521046	20040401
	CN 1764457	A	20060426	CN 2004-80008035	20040401
	EP 1660086	A2	20060531	EP 2004-725099	20040401
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
	JP 2006522084	T	20060928	JP 2006-506077	20040401
	US 2006183764	A1	20060817	US 2005-552367	20051003
PRAI	GB 2003-7863	A	20030404		
	WO 2004-GB1435	A	20040401		

IT 500355-52-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(growth hormone secretagogue-phosphodiesterase 4 inhibitor combination for treatment of Alzheimer's disease)

RN 500355-52-2 CAPLUS

CN 1,8-Naphthyridine-3-carboxamide, N-cyclopropyl-1,4-dihydro-1-[3-[2-(1-oxido-3-pyridinyl)ethynyl]phenyl]-4-oxo- (CA INDEX NAME)



L4 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB In one aspect, the present invention is directed to a one pot method of

preparing intermediates I [OR1 = a suitable leaving group; R3 = (un)substituted alkyl, aryl, heteroaryl], which are useful in making inhibitors of phosphodiesterase-4. The present invention is also directed to a method of preparing phosphodiesterase inhibitors (no biol. data given) comprising the compds. II and III which comprises reacting IV [OR1 as above] with a 3-bromopyridine-N-oxide.HCl or 3-bromopyridine in the presence of a palladium catalyst and a phosphine ligand in amine base followed by reaction of the resulting V or VI with cyclopropylamine, optionally in the presence of catalyst. Thus, reacting IV [R1 = Et] with a 3-bromopyridine-N-oxide.HCl in the presence of [(allyl)PdCl]2, P(tert-Bu)3, tert-amylamine in DMAc followed by reacting V [R1 = Et] with cyclopropylamine afforded II. Preparation of 77 aryl substituted 1,8-naphthyridin-4(1H)-ones and their intermediates is also described.

AN 2004:467891 CAPLUS
DN 141:38597
TI Preparation of aryl substituted 1,8-naphthyridin-4(1H)-ones as inhibitors of phosphodiesterase-4
IN Albaneze-Walker, Jennifer; Murry, Jerry Anthony; Soheili, Arash; Springfield, Shawn A.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 142 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004048377	A2	20040610	WO 2003-US36806	20031118
	WO 2004048377	A3	20040902		
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	CA 2506656	A1	20040610	CA 2003-2506656	20031118
	AU 2003291050	A1	20040618	AU 2003-291050	20031118
	EP 1565466	A2	20050824	EP 2003-783636	20031118
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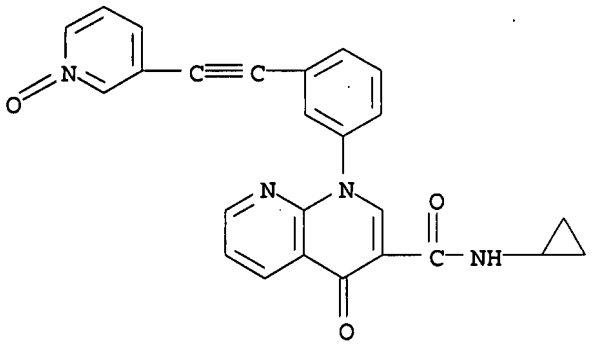
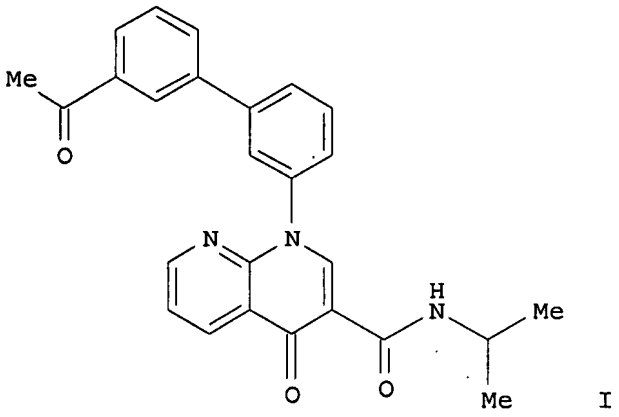
	BR 2003016464	A	20051011	BR 2003-16464	20031118
	CN 1738818	A	20060222	CN 2003-80108946	20031118
	JP 2006513271	T	20060420	JP 2005-510366	20031118
	US 2006019981	A1	20060126	US 2005-530465	20050405
	NO 2005003047	A	20050810	NO 2005-3047	20050621
PRAI	US 2002-428315P	P	20021122		
	US 2003-472655P	P	20030522		
	WO 2003-US36806	W	20031118		

OS MARPAT 141:38597
IT 500355-52-2P
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aryl substituted 1,8-naphthyridin-4(1H)-ones as inhibitors of phosphodiesterase-4)

RN 500355-52-2 CAPLUS
CN 1,8-Naphthyridine-3-carboxamide, N-cyclopropyl-1,4-dihydro-1-[3-[2-(1-oxido-3-pyridinyl)ethynyl]phenyl]-4-oxo- (CA INDEX NAME)



L4 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
GI



AB Substituted naphthyridines are prepared as PDE-4 inhibitors. For instance, Et 3-(3-bromoanilino)-2-(2-chloronicotinoyl)acrylate (preparation given) is treated with NaH in THF to give Et 1-(3-bromophenyl)-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxylate. This intermediate is saponified, coupled to i-PrNH2 (THF, Et3N, i-BuOCOCl) and coupled to 3-acetylphenylboronic acid (PhMe, EtOH, Na2CO3, trans-dibromobis(triphenylphosphine)palladium, reflux, 1 h) to give I. Example compds. have IC50 values of 0.1 to 90.0 nM for PDE4; these compds. are useful for enhancing memory, learning, retention, recall, awareness and judgement.
AN 2004:467741 CAPLUS
DN 141:38595
TI Preparation of substituted naphthyridine phosphodiesterase-4 inhibitors as enhancers of cognition
IN Dube, Daniel; Gallant, Michel; Lacombe, Patrick; Girard, Yves; MacDonald,

Dwight; Friesen, Richard; Ducharme, Yves; Cote, Bernard; Blouin, Marc; Martins, Evelyn; Guay, Daniel; Girard, Mario; Frenette, Richard; Laliberte, Sebastien; Robichaud, Annette; Mastracchio, Anthony; Perrier, Helene

PA Merck Frosst Canada & Co., Can.; Hamel, Pierre

SO PCT Int. Appl., 138 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004047836	A1	20040610	WO 2003-CA1799	20031119
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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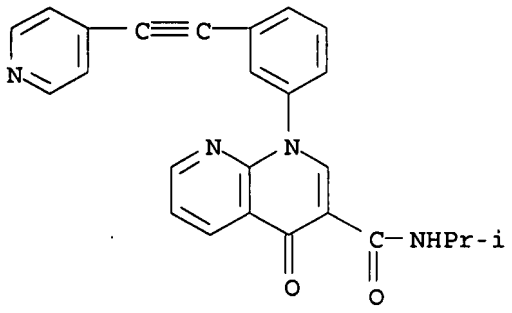
AU 2003286024	A1	20040618	AU 2003-286024	20031119
EP 1592419	A1	20051109	EP 2003-776698	20031119
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2006040981	A1	20060223	US 2005-536250	20050520
PRAI US 2002-428541P	P	20021122		
WO 2003-CA1799	W	20031119		

IT 500355-39-5P, N-Isopropyl-1-[3-[(pyridin-4-yl)ethynyl]phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of substituted naphthyridine phosphodiesterase-4 inhibitors as enhancers of cognition)

RN 500355-39-5 CAPLUS

CN 1,8-Naphthyridine-3-carboxamide, 1,4-dihydro-N-(1-methylethyl)-4-oxo-1-[3-(4-pyridinylethynyl)phenyl]- (9CI) (CA INDEX NAME)



RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN

AB The title 1-phenyl-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide derivs. are prepared as phosphodiesterase 4 (PDE4) inhibitors. For example, N-isopropyl-1-[3-(phenylethynyl)phenyl]-1,4-dihydro-[1,8]naphthyridin-4-one-3-carboxamide was prepared in a multi-step synthesis comprising a ring-closure reaction. The title compds., in conjunction with psychotherapy, provide enhanced therapeutic results in the treatment of psychiatric disorders including specific phobias, panic disorders, anxiety disorders including posttraumatic stress disorders, and obsessive-compulsive disorder (no data).

AN 2004:452951 CAPLUS

DN 141:23432

TI Preparation of 1-phenyl-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide derivatives as PDE4 inhibitors for treatment of psychiatric disorders

IN Scolnick, Edward M.

PA Merck & Co., Inc., USA

SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004045508	A2	20040603	WO 2003-US35718	20031110
	WO 2004045508	A3	20050324		
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	AU 2003291418	A1	20040615	AU 2003-291418	20031110
	EP 1562588	A2	20050817	EP 2003-768815	20031110
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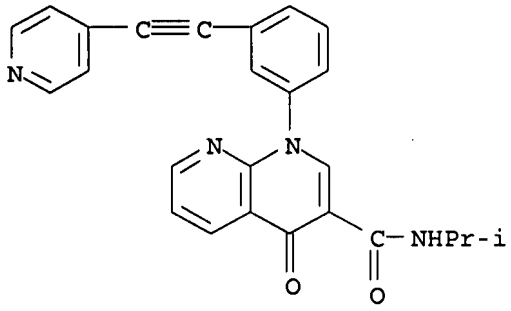
	US 2006069115	A1	20060330	US 2005-530841	20050408
PRAI	US 2002-426529P	P	20021115		
	WO 2003-US35718	W	20031110		

IT 500355-39-5P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of dihydro[1,8]naphthyridinone derivs. as PDE4 inhibitors for treatment of psychiatric disorders)

RN 500355-39-5 CAPLUS

CN 1,8-Naphthyridine-3-carboxamide, 1,4-dihydro-N-(1-methylethyl)-4-oxo-1-[3-(4-pyridinylethynyl)phenyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
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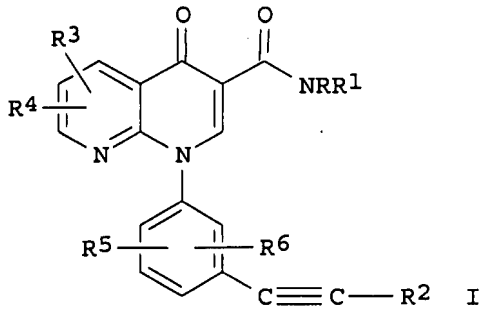

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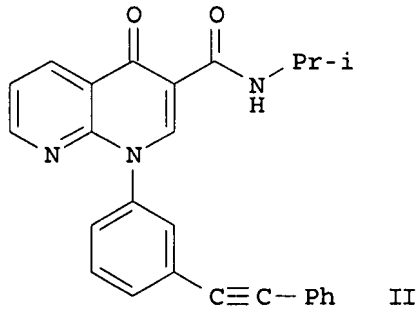

II

AB Alkyne-aryl 1,8-naphthyridin-4(1H)ones of formula I [R = H, alkyl, cycloalkyl; R1 = H, alkyl, cycloalkyl, alkoxy, acyl, Ph, heteroaryl, etc.; R2 = H, (substituted) Ph, pyridyl, pyrimidinyl, indolyl, quinolinyl, thienyl, etc. and oxides thereof; R3-R6 = H, halo, alkyl, alkoxy, nitro, CN, etc.] are prepared as phosphodiesterase 4 inhibitors useful in the treatment of asthma and inflammation. Thus, II was prepared from Et 2-chloronicotinoyl acetate, 3-bromoaniline, isopropylamine and phenylacetylene. The prepared compds. inhibited the hydrolysis of cAMP with IC50 of 0.1 nM to 90.0 nM.

AN 2003:173603 CAPLUS
DN 138:205042
TI Preparation of alkyne-aryl 1,8-naphthyridin-4(1H)ones as phosphodiesterase-4 inhibitors
IN Guay, Daniel; Girard, Mario; Hamel, Pierre; Laliberte, Sebastien; Friesen, Richard
PA Merck Frosst Canada & Co., Can.
SO PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003018579	A1	20030306	WO 2002-CA1324	20020827

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US 2005070569	A1	20050331	US 2004-487047	20040217	
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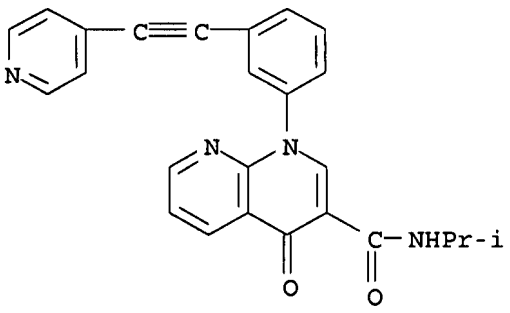
NO 2004001293	A	20040527	NO 2004-1293	20040326	
PRAI US 2001-316093P	P	20010829			
WO 2002-CA1324	W	20020827			

OS MARPAT 138:205042

IT 500355-39-5P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of alkyne-aryl naphthyridinones as phosphodiesterase 4 inhibitors)

RN 500355-39-5 CAPLUS

CN 1,8-Naphthyridine-3-carboxamide, 1,4-dihydro-N-(1-methylethyl)-4-oxo-1-[3-(4-pyridinylethynyl)phenyl]- (9CI) (CA INDEX NAME)



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